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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/593,900	09/22/2006	Han Oh Park	27681U	5781

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THE NATH LAW GROUP
112 South West Street
Alexandria, VA 22314

EXAMINER

STRZELECKA, TERESA E

ART UNIT	PAPER NUMBER
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1637

MAIL DATE	DELIVERY MODE
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04/27/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/593,900	Applicant(s) PARK ET AL.	
	Examiner TERESA E. STRZELECKA	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 February 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-34 is/are pending in the application.
- 4a) Of the above claim(s) 9-34 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7 is/are rejected.
- 7) ☒ Claim(s) 8 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>12/22/06</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I (claims 1-8, SEQ ID NO: 16) in the reply filed on February 27, 2009 is acknowledged. The traversal is on the ground(s) that:

A) The claims share a special technical feature of a "fluorescent probe for real-time detection of amplification of nucleic acid wherein a fluorescent dye of which intensity of fluorescence is varied when the dye is intercalated into a double-stranded nucleic acid, is connected with an oligonucleotide of which base sequence is complementary with at least a part of said nucleic acid.", which is "...novel and superior to the nucleic acid probe disclosed in Mergny et al."

B) Groups I-III should be examined together because the restriction requirement is improper on the basis of the unity of invention and it does not contain an appropriate explanation as to the existence of a serious burden if the restriction was not required.

C) The election of species requirement is not proper because sequences with SEQ ID NO: 8-17, 21 and 22 have a common property/activity in that they can be connected with a fluorescent dye and are designed based on the same sequence.

This is not found persuasive because:

A) The claimed probe of claim 1 is not novel as compared to the probe of Mergny et al., as detailed in the restriction requirement and in the rejection presented below. The superiority part is not relevant to the fact that the probe as claimed is anticipated. Therefore, the restriction is proper as there is no unifying special technical feature.

B) The national phase applications are governed by the Unity of Invention rules of the PCT (see MPEP 1850), which do not require an explanation of why a search and examination burden exists in examining all of the claimed invention. However, there is no problem in providing

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Applicants with an explanation: Claims of Group I are drawn to a very large genus of oligonucleotides whose only structural requirement is having a fluorescent dye associated with it. There is no requirement that the dye even be covalently bound to the oligonucleotide. Therefore these claims read on literally thousands of different oligonucleotides, either single or double-stranded, associated either covalently or non-covalently with a fluorescent dye. Such oligonucleotides are not necessarily used in amplification reactions or in real-time PCR, but can be used as hybridization probes, for example. Therefore, search for the probes of Group I is not coextensive with a search for the methods and compositions of Groups II and III.

C) The sequences are claimed as a Markush group, not as a set of sequences, therefore Applicants were asked to elect one for examination. If Applicants so wish, once one sequence is found allowable, the search will be extended to another sequence. Further, there is a significant search burden associated with searching multiple sequences by the Patent Office.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 9-34 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim.

Applicant timely traversed the restriction (election) requirement in the reply filed on February 27, 2009.

3. Claims 1-8 will be examined. Claim 8 will be examined to the degree that it reads on SEQ ID NO: 16.

Information Disclosure Statement

4. The information disclosure statement (IDS) submitted on December 22, 2006 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Specification

5. The abstract of the disclosure is objected to because some of the numbers referring to temperatures in the method steps read as 931C, 961C, 571C, 701C, etc., therefore these cannot be amplification temperatures. Correction is required. See MPEP § 608.01(b).

Claim Interpretation

6. The term "base" is interpreted as "nucleotide", since Applicants did not define it, and the claims and specification seem to use it in this context.

7. The limitation of claim 1 "for real-time detection of amplification of nucleic acid" is not taken into account when comparing the claimed product with the prior art, since it is an intended use limitation and does not impart any further structural limitation on the claimed product. Therefore the structure claimed in claim 1 is an oligonucleotide with a fluorescent dye attached to it either covalently or non-covalently.

8. The limitation of claim 6 is not taken into account when comparing the claimed oligonucleotide with prior art, since it refers to an intended use of the oligonucleotide and does not impart any further structural limitation on the claimed product.

9. The term "composed of" is interpreted as "comprising".

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claim 4 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in

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the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding genus/species situations that "Satisfactory disclosure of a ``representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.)

All of the current claims encompass a genus of fluorescent dyes which are different from the ones disclosed in the specification or known in the prior art. While the fluorescent dyes such as acridine, acridine orange, actinomycin, etc. are known in the art, Applicants have not described a single derivative of any of the claimed 19 fluorescent dyes. Therefore the genus includes variants for which no written description is provided in the specification. This large genus is represented in the specification by only the particularly named fluorescent dyes known in the art. Thus, applicant has express possession of only 19 fluorescent dyes, in a genus which comprises hundreds of millions of different possibilities. Here, no common element or attributes of the structures are disclosed, not even the presence of certain functional groups. No structural limitations or requirements which provide guidance on the identification of structures which meet these functional limitations is provided.

In Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

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"...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any fluorescent dyes other than those expressly disclosed. Therefore, the claims fail to meet the written description requirement by encompassing structures which are not described in the specification.

Finally, as stated in *In re Ruschig, Aumuller, Korger, Wagner, Scholz, and Bander*, 154 USPQ 118 (C.C.P.A. 1967):

"It is an old custom in the woods to mark trails by making blaze marks on the trees. It is no help in finding a trail or in finding one's way through the woods where the trails have disappeared- or have not yet been made, which is more like the case here-to be confronted simply by a large number of unmarked trees. Appellants are pointing to trees. We are looking for blaze marks which single out particular trees. We see none." (page 123).

In other words, Applicants have provided structures of known fluorescent dyes, but have not provided any direction or guidance as how to obtain any of the claimed derivatives, Or even what such derivatives may be.

12. Claim 4 is rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. The term "derivative" used with respect to all of the claimed fluorescent dyes critical or essential to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976).

Applicants have not provided any structures of the derivatives of fluorescent dyes claimed or guidance of how to obtain such derivatives.

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claim 6 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 recites the limitation "said primer" in line 3. There is insufficient antecedent basis for this limitation in the claim. Claim 1, from which claim 6 depends, does not contain a limitation "a primer".

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 1-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Mergny et al. (Nucl. Acids Res., vol. 22, pp. 920-928, 1994; cited in the previous office action) as evidenced by Morgan et al. (Nucl. Acids Res., vol. 7, pp. 547-569, 1979).

Regarding claims 1 and 6, Mergny et al. teach an oligonucleotide probe with a fluorescent dye, such as ethidium bromide, attached to it (page 921, sixth paragraph; Fig. 1). As evidenced by Morgan et al. (page 547, first paragraph), fluorescence of ethidium bromide increases when it is bound to double-stranded DNA.

Regarding claim 2, Mergny et al. teach the fluorescent dye connected either at the 3'- or 5'-ends (page 921, sixth paragraph; Fig. 1).

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Regarding claim 3, Mergny et al. teach the fluorescent dye connected either at the 3'- or 5'-ends (page 921, sixth paragraph; Fig. 1). Therefore, the oligonucleotides with the 3'-ends bound to the dye will not be amenable to extension by a polymerase.

Regarding claim 4, Mergny et al. teach ethidium bromide and acridine (Fig. 1).

Regarding claim 5, Mergny et al. teach the fluorescent dye connected covalently either at the 3'- or 5'-ends (page 921, sixth paragraph; Fig. 1).

Regarding claim 7, Mergny et al. teach 11-mers and 14-mers (Fig. 1), anticipating the range between 10 and 40 bp.

Allowable Subject Matter

17. Claim 8 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. No references were found teaching or suggesting SEQ ID NO: 16, therefore claim 8 is allowable if re-written to reflect this fact.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TERESA E. STRZELECKA whose telephone number is (571)272-0789. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Teresa E Strzelecka
Primary Examiner
Art Unit 1637

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Primary Examiner, Art Unit 1637
April 22, 2009